

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 18 May 2001 (18.05.01)	
<b>International application No.</b> PCT/US00/19821	<b>Applicant's or agent's file reference</b> 30431.7WO01
<b>International filing date (day/month/year)</b> 19 July 2000 (19.07.00)	<b>Priority date (day/month/year)</b> 19 July 1999 (19.07.99)
<b>Applicant</b> GRAY, Harry, B. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 15 February 2001 (15.02.01)

☐ in a notice effecting later election filed with the International Bureau on:  
 \_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Nestor Santesso Telephone No.: (41-22) 338.83.38
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The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EPO

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:  
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only

Identification of IPEA		Date of receipt of DEMAND
<b>Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION</b>		Applicant's or agent's file reference
International application No. PCT/US00/19821	International filing date (day/month/year) 19 July 2000	(Earliest) Priority date (day/month/year) 19 July 1999
Title of invention DETECTION OF BIOMOLECULES BY SENSITIZER-LINKED SUBSTRATES		
<b>Box No. II APPLICANT(S)</b>		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  California Institute of Technology 1200 East California Boulevard Pasadena, California 91125 United States of America		Telephone No.: (626) 395-4567
		Facsimile No.: (626) 577-2528
		Teleprinter No.:
State (that is, country) of nationality: US	State (that is, country) of residence: US	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  GRAY, Harry B. 1415 East California Boulevard Pasadena, California 91106 United States of America		
State (that is, country) of nationality: US	State (that is, country) of residence: US	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  CRANE, Brian R. 719 N. Aurora Street Ithaca, New York 14850 United States of America		
State (that is, country) of nationality: US	State (that is, country) of residence: US	
<input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.		

## Continuation of Box No. II APPLICANT(S)

*If none of the following sub-boxes is used, this sheet should not be included in the demand.*

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

WINKLER, Jay R.  
1110 N. Chester Avenue  
Pasadena, California 91104  
United States of America

State *(that is, country)* of nationality:

US

State *(that is, country)* of residence:

US

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

DMOCHOWSKI, Ivan Julian  
97 N. Holliston Avenue  
Pasadena, California 91106  
United States of America

State *(that is, country)* of nationality:

US

State *(that is, country)* of residence:

US

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

WILKER, Jonathan J.  
2421 Kestral Boulevard  
West Lafayette, Indiana 47906  
United States of America

State *(that is, country)* of nationality:

US

State *(that is, country)* of residence:

US

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:



Further applicants are indicated on another continuation sheet.

**Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**The following person is ☒ agent ☐ common representativeand ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*ADRIANO, Sarah B.  
Mandel & Adriano  
35 N. Arroyo Parkway, Suite 60  
Pasadena, California 91103  
United States of America

Telephone No.:

(626) 395-7801

Facsimile No.:

(626) 395-0694

Teleprinter No.:

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION****Statement concerning amendments: \***

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filedthe description ☒ as originally filed☐ as amended under Article 34the claims ☒ as originally filed☐ as amended under Article 19 (together with any accompanying statement)☐ as amended under Article 34the drawings ☒ as originally filed☐ as amended under Article 342. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

\* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

**Language for the purposes of international preliminary examination: English**☒ which is the language in which the international application was filed.☐ which is the language of a translation furnished for the purposes of international search.☐ which is the language of publication of the international application.☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.**Box No. V ELECTION OF STATES**The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

## Box No. VI. CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- |  |   |        |
|--|---|--------|
| 1. translation of international application                              | : | sheets |
| 2. amendments under Article 34   | : | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19  | : | sheets |
| 5. letter  | : | sheets |
| 6. other ( <i>specify</i> )  | : | sheets |

For International Preliminary Examining Authority use only

received                      not received

<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

- |  |   |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet                             | 4. <input type="checkbox"/> statement explaining lack of signature                                  |
| 2. <input type="checkbox"/> separate signed power of attorney                            | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input checked="" type="checkbox"/> other ( <i>specify</i> ): transmittal sheet, postcard, check |

## Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

*Sarah B. Adriano*

Sarah B. Adriano  
Reg. No. 34,470

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. ☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

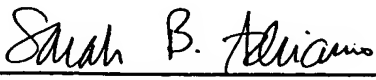
For International Bureau use only

Demand received from IPEA on:

## PCT

## FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No. <b>PCT/US00/19821</b>	For International Preliminary Examining Authority use only	
Applicant's or agent's file reference <b>30431.7WO01</b>	Date stamp of the IPEA	
Applicant  <div style="text-align: center;">California Institute of Technology et al.</div>		
<b>Calculation of prescribed fees</b>  <div style="display: flex; justify-content: space-between;"> <div style="width: 60%;">           1. Preliminary examination fee .....         </div> <div style="width: 35%; text-align: right;"> <div style="border: 1px solid black; padding: 2px 10px;">750</div> <div style="border: 1px solid black; padding: 2px 5px; float: right;">P</div> </div> </div> <div style="display: flex; justify-content: space-between;"> <div style="width: 60%;">           2. Handling fee <i>(Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.)</i> .....         </div> <div style="width: 35%; text-align: right;"> <div style="border: 1px solid black; padding: 2px 10px;">137</div> <div style="border: 1px solid black; padding: 2px 5px; float: right;">H</div> </div> </div> <div style="display: flex; justify-content: space-between;"> <div style="width: 60%;">           3. Total of prescribed fees            Add the amounts entered at P and H            and enter total in the TOTAL box .....         </div> <div style="width: 35%; text-align: right;"> <div style="border: 1px solid black; padding: 2px 10px;">887</div> <div style="border: 1px solid black; padding: 2px 10px; margin-top: 5px;">TOTAL</div> </div> </div>		
<b>Mode of Payment</b>  <div style="display: flex; flex-wrap: wrap;"> <div style="width: 50%;"> <input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)         </div> <div style="width: 50%;"> <input type="checkbox"/> cash         </div> <div style="width: 50%;"> <input checked="" type="checkbox"/> cheque         </div> <div style="width: 50%;"> <input type="checkbox"/> revenue stamps         </div> <div style="width: 50%;"> <input type="checkbox"/> postal money order         </div> <div style="width: 50%;"> <input type="checkbox"/> coupons         </div> <div style="width: 50%;"> <input type="checkbox"/> bank draft         </div> <div style="width: 50%;"> <input type="checkbox"/> other (specify):         </div> </div>		
<b>Deposit Account Authorization</b> <i>(this mode of payment may not be available at all IPEAs)</i>  The IPEA/ EPO <input type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account.  <input checked="" type="checkbox"/> <i>(this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)</i> is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.		
50-0306 Deposit Account Number	2/15/01 Date (day/month/year)	 Signature Sarah B. Adriano

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 05 NOV 2001

WIPO

PCT

Applicant's or agent's file reference 30431.7WO01	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/19821	International filing date (day/month/year) 19 July 2000 (19.07.2000)	Priority date (day/month/year) 19 July 1999 (19.07.1999)
International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 33/53, 33/542; C12Q 1/26 and US Cl.: 435/4, 7.1, 7.9, 7.92, 25, 175; 436/518, 537, 544		
Applicant CALIFORNIA INSTITUTE OF TECHNOLOGY		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand 15 February 2001 (15.02.2001)	Date of completion of this report 02 October 2001 (02.10.2001)	
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Marti Padmanathan Telephone No. 703-308-0196	

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.

PCT/US00/19821

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-110 \_\_\_\_\_ as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 111-114 \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, as amended (together with any statement) under Article 19  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the drawings:  
pages 1-54 \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☐ the sequence listing part of the description:  
pages NONE \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☒ The amendments have resulted in the cancellation of:**

- ☐ the description, pages NONE
- ☒ the claims, Nos. 1-19
- ☐ the drawings, sheets/fig NONE

**5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.  
PCT/US98/019821**V. Reasoned statement under Rule 66.2(a)(II) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-37</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-37</u>	NO
Industrial Applicability (IA)	Claims <u>1-37</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-37 lack novelty under PCT Article 33(2) as being anticipated by Wilker et al. (Angew. Chem. Int. Ed., Jan 1999).

Wilker et al. disclose substrates for rapid delivery of electrons and holes to buried active sites in proteins. The reference discloses a photochemical method for this purpose by tethering a Ru photosensitizer to a protein substrate, which reduces the P450 heme very rapidly. By linking sensitizers to substrates, the reactive redox states in enzyme interiors can be studied more closely. The photosensitizer  $[Ru(bpy)_3]^{2+}$  is linked through a hydrocarbon chain to a species with high affinity for the P450 heme pocket (imidazole, adamantane, or ethylbenzene). Laser excitation of  $Ru^{II}-Im$  followed by reductive quenching yields a powerful reductant,  $Ru^I-Im$ . In the presence of P450, the reductant is converted rapidly to  $Ru^{II}-Im$ . This oxidation occurs at the same time as reduction of the heme group. The use of sensitizer-linked substrates allows the preparation of new oxidized and reduced states of P450.

It is noted that any limitations present in the specification are not given patentable weight, as they do not appear in the claims. Further, applicant's arguments that the Wilker reference does not disclose or teach the use of sensitizer-linked substrates to detect and/or characterize biomolecules are unconvincing. The biomolecules of the present application includes P450, and the reference clearly discloses binding and detection of P450. Molecules such as Ru-Ad or Ru-Im bind P450, and the absorption spectra are obtained.

# PATENT COOPERATION TREATY

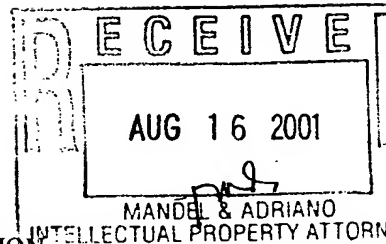
From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:  
SARAH B. ADRIANO  
MANDEL & ADRIANO  
35 NO. ARROYO PARKWAY  
SUITE 60  
PASADENA, CA 91103

**PCT**

WRITTEN OPINION

(PCT Rule 66)



Applicant's or agent's file reference <b>30431.7WO01</b>		Date of Mailing (day/month/year) <b>10 AUG 2001</b>
International application No. <b>PCT/US00/19821</b>		REPLY DUE within 1 months/days from the above date of mailing
International filing date (day/month/year) <b>19 July 2000 (19.07.2000)</b>	Priority date (day/month/year) <b>19 July 1999 (19.07.1999)</b>	
International Patent Classification (IPC) or both national classification and IPC <b>IPC(7): G01N 33/53, 33/542; C12Q 1/26 and US Cl.: 435/4, 7.1, 7.9, 7.92, 25, 175; 436/518, 537, 544</b>		
Applicant <b>CALIFORNIA INSTITUTE OF TECHNOLOGY</b>		

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
  - I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application
3. The applicant is hereby **invited to reply** to this opinion.
 

**When?** See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also** For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.  
For an informal communication with the examiner, see Rule 66.6

**If no reply is filed**, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 19 October 2001 (19.10.2001)

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Kartic Padmanabhan Telephone No. 703-308-0196
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**I. Basis of the opinion****1. With regard to the elements of the international application:\***

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-110, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 111-114, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages 1-54, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:**

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☐ The amendments have resulted in the cancellation of:**

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

**5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."

WRITTEN OPINION

International application No.  
PCT/US00/19821

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. STATEMENT**

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-37</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-37</u>	NO
Industrial Applicability (IA)	Claims <u>1-37</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-37 lack novelty under PCT Article 33(2) as being anticipated by Wilker et al. (Angew. Chem. Int. Ed., Jan 1999).

Wilker et al. disclose substrates for rapid delivery of electrons and holes to buried active sites in proteins. The reference discloses a photochemical method for this purpose by tethering a Ru photosensitizer to a protein substrate, which reduces the P450 heme very rapidly. By linking sensitizers to substrates, the reactive redox states in enzyme interiors can be studied more closely. The photosensitizer  $[Ru(bpy)_3]^{2+}$  is linked through a hydrocarbon chain to a species with high affinity for the P450 heme pocket (imidazole, adamantane, or ethylbenzene). Laser excitation of  $Ru^{II}$ -Im followed by reductive quenching yields a powerful reductant,  $Ru^I$ -Im. In the presence of P450, the reductant is converted rapidly to  $Ru^{II}$ -Im. This oxidation occurs at the same time as reduction of the heme group. The use of sensitizer linked substrates allows the preparation of new oxidized and reduced states of P450.

WRITTEN OPINION

International application No.  
PCT/US00/19821

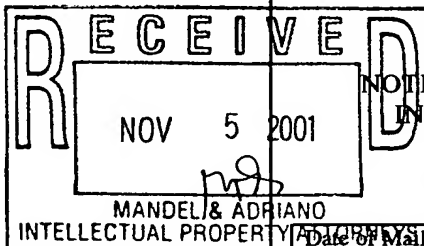
**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

**TIME LIMIT:**

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

## TENT COOPERATION TREATY

RECEIVED  
NOV 09 2001  
GRAYCARY/GT.PATENTFrom the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITYTo:  
SARAH B. ADRIANO  
MANDEL & ADRIANO  
35 NO. ARROYO PARKWAY  
SUITE 60  
PASADENA, CA 91103

PCT

NOTIFICATION OF TRANSMITTAL OF  
INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing  
(day/month/year)

31 OCT 2001

Applicant's or agent's file reference

30431.7WO01

IMPORTANT NOTIFICATION

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US00/19821

19 July 2000 (19.07.2000)

19 July 1999 (19.07.1999)

Applicant

CALIFORNIA INSTITUTE OF TECHNOLOGY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Kartik Padmanabhan

Telephone No. 703-308-0196


Form PCT/IPEA/416 (July 1992)

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 30431.7WO01	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/19821	International filing date ( <i>day/month/year</i> ) 19 July 2000 (19.07.2000)	Priority date ( <i>day/month/year</i> ) 19 July 1999 (19.07.1999)
International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 33/53, 33/542; C12Q 1/26 and US Cl.: 435/4, 7.1, 7.9, 7.92, 25, 175; 436/518, 537, 544		
Applicant CALIFORNIA INSTITUTE OF TECHNOLOGY		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>		
Date of submission of the demand 15 February 2001 (15.02.2001)	Date of completion of this report 02 October 2001 (02.10.2001)	
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer  Ratic Padmanabhan Telephone No. 703-308-0196	

Form PCT/IPEA/409 (cover sheet)(July 1998)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.

PCT/US00/19821

**I. Basis of the report**

## 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-110 as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 111-114 as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the drawings:  
pages 1-54 as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☐ the sequence listing part of the description:  
pages NONE as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☒ the claims, Nos. 1-19
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US00/19821**V. Reasoned statement under Rule 66.2(a)(II) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-37</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-37</u>	NO
Industrial Applicability (IA)	Claims <u>1-37</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-37 lack novelty under PCT Article 33(2) as being anticipated by Wilker et al. (Angew. Chem. Int. Ed., Jan 1999).

Wilker et al. disclose substrates for rapid delivery of electrons and holes to buried active sites in proteins. The reference discloses a photochemical method for this purpose by tethering a Ru photosensitizer to a protein substrate, which reduces the P450 heme very rapidly. By linking sensitizers to substrates, the reactive redox states in enzyme interiors can be studied more closely. The photosensitizer  $[Ru(bpy)_3]^{2+}$  is linked through a hydrocarbon chain to a species with high affinity for the P450 heme pocket (imidazole, adamantane, or ethylbenzene). Laser excitation of  $Ru^{II}$ -Im followed by reductive quenching yields a powerful reductant,  $Ru^I$ -Im. In the presence of P450, the reductant is converted rapidly to  $Ru^{II}$ -Im. This oxidation occurs at the same time as reduction of the heme group. The use of sensitizer-linked substrates allows the preparation of new oxidized and reduced states of P450.

It is noted that any limitations present in the specification are not given patentable weight, as they do not appear in the claims. Further, applicant's arguments that the Wilker reference does not disclose or teach the use of sensitizer-linked substrates to detect and/or characterize biomolecules are unconvincing. The biomolecules of the present application includes P450, and the reference clearly discloses binding and detection of P450. Molecules such as Ru-Ad or Ru-Im bind P450, and the absorption spectra are obtained.

# PCT REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only
International Application No. <span style="float: right; font-size: 1.2em;">10/030861</span>
International Filing Date
Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference (if desired) (12 characters maximum) 30431.7WO01
--

<b>Box No. I TITLE OF INVENTION</b> DETECTION OF BIOMOLECULES BY SENSITIZER-LINKED SUBSTRATES	
<b>Box No. II APPLICANT</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.) California Institute of Technology 1200 East California Boulevard Pasadena, California 91125 United States of America	<input type="checkbox"/> This person is also inventor. <hr/> Telephone No. 626/395-4567 <hr/> Facsimile No. 626/577-2528 <hr/> Teleprinter No.
State (i.e. country) of nationality: US	State (i.e. country) of residence: US
This person is applicant <input type="checkbox"/> all designated <input checked="" type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<b>Box No. III FURTHER APPLICANT(S) AND /OR (FURTHER) INVENTOR(S)</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.) GRAY, Harry B. 1415 East California Boulevard Pasadena, California 91106 United States of America	This person is : <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input checked="" type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (i.e. country) of nationality: US	State (i.e. country) of residence: US
This person is applicant <input type="checkbox"/> all designated <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<input checked="" type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet.	
<b>Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE</b>	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) ADRIANO, Sarah B. Mandel & Adriano 35 No. Arroyo Parkway, Suite 60 Pasadena, California 91103 United States of America	Telephone No. 626/ 395-7801 <hr/> Facsimile No. 626/ 395-0694 <hr/> Teleprinter No.
<input type="checkbox"/> Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.	

**Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS***If none of the following sub-boxes is used, this sheet is not to be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.)

CRANE, Brian R.  
719 N. Aurora Street  
Ithaca, New York  
United States of America

This person is :

- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
US

State (i.e. country) of residence:  
US

This person is applicant ☐ all designated ☐ all designated States except ☐ the United States ☐ the States indicated in for the purpose of: ☐ States ☐ the United States of America ☒ of America only ☐ the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.)

WINKLER, Jay R.  
1110 N. Chester Avenue  
Pasadena, California 91104  
United States of America

This person is :

- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
US

State (i.e. country) of residence:  
US

This person is applicant ☐ all designated ☐ all designated States except ☐ the United States ☐ the States indicated in for the purpose of: ☐ States ☐ the United States of America ☒ of America only ☐ the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.)

DMOCHOWSKI, Ivan Julian  
97 N. Holliston Avenue  
Pasadena, California 91106  
United States of America

This person is :

- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
US

State (i.e. country) of residence:  
US

This person is applicant ☐ all designated ☐ all designated States except ☐ the United States ☐ the States indicated in for the purpose of: ☐ States ☐ the United States of America ☒ of America only ☐ the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.)

WILKER, Jonathan J.  
2421 Kestral Boulevard  
West Lafayette, Indiana 47906  
United States of America

This person is :

- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
US

State (i.e. country) of residence:  
US

This person is applicant ☐ all designated ☐ all designated States except ☐ the United States ☐ the States indicated in for the purpose of: ☐ States ☐ the United States of America ☒ of America only ☐ the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

**Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS***If none of the following sub-boxes is used, this sheet is not to be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.)

DUNN, Alexander Robert  
4495 Terrell Lane  
Colorado Springs, Colorado 80908  
United States of America

This person is :

- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
US

State (i.e. country) of residence:  
US

This person is applicant for the purpose of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.)

This person is :

- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purpose of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.)

This person is :

- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purpose of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country of residence if no State of residence is indicated below.)

This person is :

- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purpose of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

**Box No. V DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

**Regional Patent**

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Cote d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

**National Patent (if other kind of protection or treatment desired, specify on dotted line):**

- |  |   |
|--|---|
| <input checked="" type="checkbox"/> AE United Arab Emirates                  | <input checked="" type="checkbox"/> LR Liberia  |
| <input checked="" type="checkbox"/> AL Albania                               | <input checked="" type="checkbox"/> LS Lesotho  |
| <input checked="" type="checkbox"/> AM Armenia                               | <input checked="" type="checkbox"/> LT Lithuania  |
| <input checked="" type="checkbox"/> AT Austria and Utility Model             | <input checked="" type="checkbox"/> LU Luxembourg   |
| <input checked="" type="checkbox"/> AU Australia                             | <input checked="" type="checkbox"/> LV Latvia   |
| <input checked="" type="checkbox"/> AZ Azerbaijan                            | <input checked="" type="checkbox"/> MA Morocco  |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina                | <input checked="" type="checkbox"/> MD Republic of Moldova  |
| <input checked="" type="checkbox"/> BB Barbados                              | <input checked="" type="checkbox"/> MG Madagascar   |
| <input checked="" type="checkbox"/> BG Bulgaria                              | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia  |
| <input checked="" type="checkbox"/> BR Brazil                                |   |
| <input checked="" type="checkbox"/> BY Belarus                               | <input checked="" type="checkbox"/> MN Mongolia   |
| <input checked="" type="checkbox"/> CA Canada                                | <input checked="" type="checkbox"/> MW Malawi   |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein  | <input checked="" type="checkbox"/> MX Mexico   |
| <input checked="" type="checkbox"/> CN China                                 | <input checked="" type="checkbox"/> NO Norway   |
| <input checked="" type="checkbox"/> CR Costa Rica                            | <input checked="" type="checkbox"/> NZ New Zealand  |
| <input checked="" type="checkbox"/> CU Cuba                                  | <input checked="" type="checkbox"/> PL Poland   |
| <input checked="" type="checkbox"/> CZ Czech Republic and Utility Model      | <input checked="" type="checkbox"/> PT Portugal   |
| <input checked="" type="checkbox"/> DE Germany and Utility Model             | <input checked="" type="checkbox"/> RO Romania  |
| <input checked="" type="checkbox"/> DK Denmark and Utility Model             | <input checked="" type="checkbox"/> RU Russian Federation   |
| <input checked="" type="checkbox"/> DM Dominica                              | <input checked="" type="checkbox"/> SD Sudan  |
| <input checked="" type="checkbox"/> EE Estonia and Utility Model             | <input checked="" type="checkbox"/> SE Sweden   |
| <input checked="" type="checkbox"/> ES Spain                                 | <input checked="" type="checkbox"/> SG Singapore  |
| <input checked="" type="checkbox"/> FI Finland and Utility Model             | <input checked="" type="checkbox"/> SI Slovenia   |
| <input checked="" type="checkbox"/> GB United Kingdom                        | <input checked="" type="checkbox"/> SK Slovakia and Utility Model   |
| <input checked="" type="checkbox"/> GD Grenada                               | <input checked="" type="checkbox"/> SL Sierra Leone   |
| <input checked="" type="checkbox"/> GE Georgia                               | <input checked="" type="checkbox"/> TJ Tajikistan   |
| <input checked="" type="checkbox"/> GH Ghana                                 | <input checked="" type="checkbox"/> TM Turkmenistan   |
| <input checked="" type="checkbox"/> GM Gambia                                | <input checked="" type="checkbox"/> TR Turkey   |
| <input checked="" type="checkbox"/> HR Croatia                               | <input checked="" type="checkbox"/> TT Trinidad and Tobago  |
| <input checked="" type="checkbox"/> HU Hungary                               | <input checked="" type="checkbox"/> TZ United Republic of Tanzania  |
| <input checked="" type="checkbox"/> ID Indonesia                             | <input checked="" type="checkbox"/> UA Ukraine  |
| <input checked="" type="checkbox"/> IL Israel                                | <input checked="" type="checkbox"/> UG Uganda   |
| <input checked="" type="checkbox"/> IN India                                 | <input checked="" type="checkbox"/> US United States of America   |
| <input checked="" type="checkbox"/> IS Iceland                               |   |
| <input checked="" type="checkbox"/> JP Japan                                 | <input checked="" type="checkbox"/> UZ Uzbekistan   |
| <input checked="" type="checkbox"/> KE Kenya                                 | <input checked="" type="checkbox"/> VN Viet Nam   |
| <input checked="" type="checkbox"/> KG Kyrgyzstan                            | <input checked="" type="checkbox"/> YU Yugoslavia   |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | <input checked="" type="checkbox"/> ZA South Africa   |
| <input checked="" type="checkbox"/> KR Republic of Korea                     | <input checked="" type="checkbox"/> ZW Zimbabwe   |
|  | Check-boxes reserved for designating States (for the purpose of a national Patent) which have become party to the PCT after issuance of this sheet: |
| <input checked="" type="checkbox"/> KZ Kazakstan                             | <input type="checkbox"/>  |
| <input checked="" type="checkbox"/> LC Saint Lucia                           | <input type="checkbox"/>  |
| <input checked="" type="checkbox"/> LK Sri Lanka                             | <input type="checkbox"/>  |

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted Under the PCT except the designation(s) of \_\_\_\_\_

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that the designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

<b>Box No. VI PRIORITY CLAIM</b>		Further priority claims are indicated in the Supplemental Box <input type="checkbox"/>	
The priority of the following earlier application(s) is hereby claimed:			
Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1) US	19 July 1999 19/07/99	60/144,488	
item (2) US	16 August 1999 16/08/99	60/149,278	
item (3) US	28 March 2000 28/03/00	60/192,703	
Mark the following check-box if the certified copy of the earlier application is to issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):			
<input checked="" type="checkbox"/> The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s) : <u>1</u>			
<b>Box No. VII INTERNATIONAL SEARCHING AUTHORITY</b>			
<b>Choice of International Searching Authority (ISA)</b> (If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used) : <b>ISA / EPO</b>			
<b>Earlier search</b> Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or translation thereof) or by reference to the search request: Country (or regional Office): _____ Date (day/month/year) : _____ Number: _____			
<b>Box No. VIII CHECK LIST</b>			
The international application contains The following number of sheets: 1. Request : 5 sheets 2. Description : 110 sheets 3. Claims : 4 sheets 4. Abstract : 1 sheets 5. Drawings : 57 sheets  <b>Total</b> : 177 sheets		This international application is accompanied by the item(s) marked below: 1. <input type="checkbox"/> separate signed power of attorney 2. <input type="checkbox"/> copy of general power of attorney 3. <input type="checkbox"/> statement explaining lack of signature 4. <input type="checkbox"/> priority document(s) identified in Box No VI as item(s); 5. <input checked="" type="checkbox"/> fee calculation sheet 6. <input type="checkbox"/> separate indications concerning deposited microorganisms 7. <input type="checkbox"/> nucleotide and/or amino acid sequence listing (diskette) 8. <input checked="" type="checkbox"/> other (specify): transmittal sheet in duplicate, postcard, cheque	
Figure No. <u>1</u> of the drawings (if any) should accompany the abstract when it is published.			
<b>Box No. IX SIGNATURE OF APPLICANT OR AGENT</b>			
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).			
By: <u>Sarah B. Adriano</u> ; Sarah B. Adriano		Date: July 19, 2000	

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings:  <input type="checkbox"/> received:  <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority specified by the applicant: <b>ISA /</b>	
6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid	

For International Bureau use only

Date of receipt of the record copy  
by the International Bureau:

# PCT

## FEE CALCULATION SHEET Annex to the Request

For receiving Office use only

International application No.

Date stamped of the receiving Office

Applicant's or agent's  
file reference 30431.7WO01

Applicant  
California Institute of Technology

### CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . 240 . T  
2. SEARCH FEE . . . . . 450 . S

International search to be carried out by EPO  
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

### 3. INTERNATIONAL FEE

#### Basic Fee

The international application contains 177 sheets.

First 30 sheets . . . . . 427 . b<sub>1</sub>  
147 x 10 = 1470 . b<sub>2</sub>  
remaining sheets additional amount

Add amounts entered at b<sub>1</sub> and b<sub>2</sub> and enter total at B . . . . . 1897 . B

#### Designation Fees

The international application contains 103 designations.

11 x 92 = 1012 . D  
number of designation fees amount of designation fee  
payable (maximum 11)

Add amounts entered at B and D and enter total at I . . . . . 2909 . I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT . . . . . 15 . P

### 5. TOTAL FEES PAYABLE

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

3614 .  
TOTAL

☐ The designation fee are not paid at this time.

### MODE OF PAYMENT

☒ authorization to charge deposit account (see below) ☐ bank draft ☐ coupons  
☒ cheque ☐ cash ☐ others (specify):  
☐ postal money order ☐ revenue stamps

### DEPOSIT ACCOUNT AUTHORIZATION (this mode of payment may not be available at all receiving Offices)

The RO/ US ☐ is hereby authorized to charge the total fees indicated above to my deposit account.  
☒ is hereby authorized to charge any deficiency or credit any overpayment in total fees indicated above in my deposit account.  
☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

50-0306  
Deposit Account Number

19/07/00  
Date (day/month/year)

Sarah B. Adriano  
Signature Sarah. B. Adriano

# INTERNATIONAL SEARCH REPORT

onal Application No

PCT/US 00/19821

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/58 G01N33/542 C12Q1/26

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J J WILKER, I J DMOCHOWSKI, J H DAWSON, J R WINKLER, H B GRAY: "Substrates for Rapid Delivery of Electrons and Holes to Buried Active Sites in Proteins" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, vol. 38, no. 1-2, 15 January 1999 (1999-01-15), pages 90-92, XP002153611 cited in the application the whole document ----- -/--	1-9, 12-17, 19-28, 31-34, 36,37

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

22 November 2000

Date of mailing of the international search report

07/12/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Hart-Davis, J



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/19821

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 41175 A (IGEN INC) 19 December 1996 (1996-12-19)  figure 1 ----	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
A	DE 44 39 347 A (BOEHRINGER MANNHEIM GMBH) 1 February 1996 (1996-02-01)  page 5, line 63 -page 6, line 18; figure 3 ----	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
P,X	DMOCHOWSKI IVAN J ET AL: "Optical detection of cytochrome P450 by sensitizer-linked substrates." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 96, no. 23, 9 November 1999 (1999-11-09), pages 12987-12990, XP002153612 Nov. 9, 1999 ISSN: 0027-8424 cited in the application the whole document ----	1-9, 12-17, 19-28, 31-34, 36, 37
A	US 5 731 147 A (WHITESIDES GEORGE M ET AL) 24 March 1998 (1998-03-24)  examples 1-17 ----	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
A	US 5 075 447 A (MUELLER FRANCIS ET AL) 24 December 1991 (1991-12-24)  the whole document ----- -/--	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/19821

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	<p>CONTZEN JOERG ET AL: "Changes in secondary structure and salt links of cytochrome P-450cam induced by photoreduction: A fourier transform infrared spectroscopic study." BIOCHEMISTRY, vol. 38, no. 49, 7 December 1999 (1999-12-07), pages 16253-16260, XP002153613 ISSN: 0006-2960 the whole document -----</p>	1-37

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/US 00/19821

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9641175 A	19-12-1996	AU 718767 B	20-04-2000
		AU 6384496 A	30-12-1996
		CA 2223027 A	19-12-1996
		EP 0871887 A	21-10-1998
		JP 11507726 T	06-07-1999
DE 4439347 A	01-02-1996	AT 193294 T	15-06-2000
		AU 690315 B	23-04-1998
		AU 3220595 A	22-02-1996
		CN 1134154 A, B	23-10-1996
		DE 59508391 D	29-06-2000
		WO 9603409 A	08-02-1996
		EP 0720614 A	10-07-1996
		ES 2148540 T	16-10-2000
		FI 961349 A	25-03-1996
		JP 2771900 B	02-07-1998
		JP 8509995 T	22-10-1996
		KR 183420 B	15-05-1999
		NO 961161 A	21-03-1996
		NZ 291154 A	24-11-1997
		US 5958783 A	28-09-1999
		AT 187732 T	15-01-2000
		AU 682278 B	25-09-1997
		AU 3164995 A	22-02-1996
		AU 689626 B	02-04-1998
		AU 3165095 A	22-02-1996
		AU 688953 B	19-03-1998
		AU 3220495 A	22-02-1996
		AU 684992 B	08-01-1998
		AU 3220695 A	22-02-1996
		CA 2195648 A	08-02-1996
		CA 2195752 A	08-02-1996
		CA 2195753 A	08-02-1996
		CN 1130910 A	11-09-1996
		CN 1152923 A	25-06-1997
		CN 1157655 A	20-08-1997
		DE 4430972 A	01-02-1996
		DE 4430973 A	01-02-1996
		DE 4430998 A	01-02-1996
		DE 4439345 A	01-02-1996
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		WO 9603651 A	08-02-1996
		WO 9603652 A	08-02-1996
		WO 9603423 A	08-02-1996
		WO 9603410 A	08-02-1996
		EP 0772616 A	14-05-1997
		EP 0774119 A	21-05-1997
		EP 0774120 A	21-05-1997
		EP 0772774 A	14-05-1997
		EP 0723551 A	31-07-1996
		ES 2143059 T	01-05-2000
		FI 961350 A	25-03-1996
		FI 970299 A	24-01-1997
US 5731147 A	24-03-1998	US 6140138 A	31-10-2000
		US 5310687 A	10-05-1994

## INTERNATIONAL SEARCH REPORT

Information on patent family members

onal Application No

PCT/US 00/19821

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5731147 A		US 5238808 A	24-08-1993
		US 5714089 A	03-02-1998
		AT 104057 T	15-04-1994
		AU 5020085 A	15-05-1986
		CA 1339835 A	21-04-1998
		DE 3587793 D	11-05-1994
		DE 3587793 T	18-08-1994
		EP 0199804 A	05-11-1986
		EP 0580979 A	02-02-1994
		HK 1007349 A	09-04-1999
		JP 2706650 B	28-01-1998
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		JP 7173185 A	11-07-1995
		JP 2710534 B	10-02-1998
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		WO 8602734 A	09-05-1986
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		US 5221605 A	22-06-1993
US 5075447 A	24-12-1991	AT 62749 T	15-05-1991
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		JP 6090201 B	14-11-1994
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		NO 853635 A, B,	18-03-1986
		NZ 213420 A	29-01-1990
		US 4745076 A	17-05-1988

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

## PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

To:

Mandel & Adriano  
Attn. ADRIANO, Sarah B.  
35 No. Arroyo Parkway, Suite 60  
Pasadena, Ca 91103  
UNITED STATES OF AMERICA

Date of mailing  
(day/month/year)

07/12/2000

Applicant's or agent's file reference

30431.7W001

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/US 00/19821

International filing date  
(day/month/year)

19/07/2000

Applicant

CALIFORNIA INSTITUTE OF TECHNOLOGY

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau.

If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Jaap Hurenkamp

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

**"Statement under article 19(1)" (Rule 46.4)**

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

**Consequence if a demand for international preliminary examination has already been filed**

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

**Consequence with regard to translation of the international application for entry into the national phase**

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>30431.7W001</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/19821</b>	International filing date (day/month/year) <b>19/07/2000</b>	(Earliest) Priority Date (day/month/year) <b>19/07/1999</b>
Applicant <b>CALIFORNIA INSTITUTE OF TECHNOLOGY</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

### 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

### 4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

### 5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.

2



None of the figures.



# INTERNATIONAL SEARCH REPORT

National Application No.

PCT/US 00/19821

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 G01N33/58 G01N33/542 C12Q1/26

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J J WILKER, I J DMOCHOWSKI, J H DAWSON, J R WINKLER, H B GRAY: "Substrates for Rapid Delivery of Electrons and Holes to Buried Active Sites in Proteins" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, vol. 38, no. 1-2, 15 January 1999 (1999-01-15), pages 90-92, XP002153611 cited in the application the whole document <div style="text-align: center;">--- -/--</div>	1-9, 12-17, 19-28, 31-34, 36,37

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

22 November 2000

Date of mailing of the international search report

07/12/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Hart-Davis, J

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 00/19821

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 41175 A (IGEN INC) 19 December 1996 (1996-12-19)  figure 1	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
A	DE 44 39 347 A (BOEHRINGER MANNHEIM GMBH) 1 February 1996 (1996-02-01)  page 5, line 63 -page 6, line 18; figure 3	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
P, X	DMOCHOWSKI IVAN J ET AL: "Optical detection of cytochrome P450 by sensitizer-linked substrates." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 96, no. 23, 9 November 1999 (1999-11-09), pages 12987-12990, XP002153612 Nov. 9, 1999 ISSN: 0027-8424 cited in the application the whole document	1-9, 12-17, 19-28, 31-34, 36, 37
A	US 5 731 147 A (WHITESIDES GEORGE M ET AL) 24 March 1998 (1998-03-24)  examples 1-17	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
A	US 5 075 447 A (MUELLER FRANCIS ET AL) 24 December 1991 (1991-12-24)  the whole document	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37

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International Application No

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	<p>CONTZEN JOERG ET AL: "Changes in secondary structure and salt links of cytochrome P-450cam induced by photoreduction: A fourier transform infrared spectroscopic study."</p> <p>BIOCHEMISTRY, vol. 38, no. 49, 7 December 1999 (1999-12-07), pages 16253-16260, XP002153613 ISSN: 0006-2960 the whole document</p> <p>-----</p>	1-37

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# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>30431.7W001</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/US 00/ 19821</b>	International filing date ( <i>day/month/year</i> ) <b>19/07/2000</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>19/07/1999</b>
Applicant  <b>CALIFORNIA INSTITUTE OF TECHNOLOGY</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.  
☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

**4. With regard to the title,**

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

**5. With regard to the abstract,**

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. The figure of the drawings to be published with the abstract is Figure No.**

- ☐ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☒ because this figure better characterizes the invention.
- 2             
☐ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/19821

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/58 G01N33/542 C12Q1/26

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J J WILKER, I J DMOCHOWSKI, J H DAWSON, J R WINKLER, H B GRAY: "Substrates for Rapid Delivery of Electrons and Holes to Buried Active Sites in Proteins" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, vol. 38, no. 1-2, 15 January 1999 (1999-01-15), pages 90-92, XP002153611 cited in the application the whole document --- -/--	1-9, 12-17, 19-28, 31-34, 36, 37



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&amp;\* document member of the same patent family

Date of the actual completion of the international search

22 November 2000

Date of mailing of the international search report

07/12/2000

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 41175 A (IGEN INC) 19 December 1996 (1996-12-19)  figure 1 ---	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
A	DE 44 39 347 A (BOEHRINGER MANNHEIM GMBH) 1 February 1996 (1996-02-01)  page 5, line 63 -page 6, line 18; figure 3 ---	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
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A	US 5 731 147 A (WHITESIDES GEORGE M ET AL) 24 March 1998 (1998-03-24)  examples 1-17 ---	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37
A	US 5 075 447 A (MUELLER FRANCIS ET AL) 24 December 1991 (1991-12-24)  the whole document --- -/--	1-3, 7-10, 12, 13, 16, 17, 19-22, 26-29, 31, 32, 36, 37



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International Application No

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